Claims

1. A drug targeting system for administration to a mammal comprising

- nanoparticles made of a polymeric material, said nanoparticles comprising said polymeric material, one or more physiologically effective substance(s) to be delivered to said mammal and one or more stabilizer(s) for said nanoparticles allowing targeting of said physiologically effective substance(s) to a specific site within or on a mammalian body; and
- a physiologically acceptable carrier and/or diluent allowing the transport of said nanoparticles to the target within said mammal after administration.

2. The drug targeting system according to claim 1, wherein said nanoparticles comprise particles of said polymeric material having a diameter below 1,000 nm, preferably between about 1 and about 1,000 nm.

3. The drug targeting system according to claim 1 ~~or claim 2~~, wherein said polymeric material is selected from the group consisting of polyacrylates, polymethacrylates, polycyanoacrylates, polyarylamides, polylactates, polyglycolates, polyanhydrates, poly-orthoesters, gelatin, polysaccharides, albumin, polystyrenes, polyvinyls, polyacrolein, polyglutaraldehydes and derivatives, copolymers and mixtures thereof.

4. The drug targeting system according to ~~any of the claims 1 to 3,~~ Claim 1 wherein said nanoparticles comprise said physiologically effective substance(s) to be delivered to said mammal in the form adsorbed, absorbed and/or incorporated thereto.

5. The drug targeting system according to ~~any of the claims 1 to 4,~~ wherein said physiologically effective substance(s) to be delivered to said mammal comprise(s) a therapeutic agent and a diagnostic agent.

6. The drug targeting system according to ~~any of the claims 1 to 5~~, wherein said physiologically effective substance(s) comprise(s) a substance which has central nervous system activity but cannot cross the blood brain barrier without modification or without a carrier.

7. The drug targeting system according to ~~any of the claims 1 to 6~~; wherein said therapeutic agent is selected from the group consisting of drugs acting at synaptic sites and neuroeffector junctional sites; general and local analgetics; hypnotics and sedatives; drugs for the treatment of psychiatric disorders such as depression and schizophrenia; anti-epileptics and anticonvulsants; drugs for the treatment of Parkinson's and Huntington's disease, aging and Alzheimer's disease; excitatory amino acid antagonists, neurotrophic factors and neuroregenerative agents; trophic factors; drugs aimed at the treatment of CNS trauma or stroke; drugs for the treatment of addiction and drug abuse; antacoids and anti-inflammatory drugs; chemotherapeutic agents for parasitic infections and diseases caused by microbes; immunosuppressive agents and anti-cancer drugs; hormones and hormone antagonists; heavy metals and heavy metal antagonists; antagonists for non-metallic toxic agents; cytostatic agents for the treatment of cancer; diagnostic substances for use in nuclear medicine; immunoactive and immunoreactive agents; transmitters and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites; transporter inhibitors; antibiotics; antispasmodics; antihistamines; antinauseants; relaxants; stimulants; sense and antisense oligonucleotides; cerebral dilators; psychotropics; antimanics; vascular dilators and constrictors; anti-hypertensives; drugs for migraine treatment; hypnotics, hyperglycemic and hypoglycemic agents; minerals and nutritional agents; anti-obesity drugs; anti-asthmatics; and mixtures thereof.

Claim 1

8. The drug targeting system according to ~~any of the claims 1 to 6~~, wherein said diagnostic agent is selected from the group consisting of diagnostics useful in the diagnosis in nuclear medicine and in radiation therapy.

Claim 1

9. The drug targeting system according to ~~any of the claims 1 to 8~~, wherein said stabilizer for said nanoparticles is selected from the group consisting of stabilizers which allow a passage of said nanoparticles including said physiologically effective substance(s) through the blood brain barrier in said mammal and stabilizers which allow a release of said physiologically effective substance(s) from said nanoparticles and a passage of said physiologically effective substance(s) through the blood brain barrier separate from said nanoparticles.

10. The drug targeting system according to claim 9, wherein said stabilizer is one allowing a passage of said physiologically effective substance(s) through the blood brain barrier without chemical modification of said physiologically effective substance(s).

Claim 1

11. The drug targeting system according to ~~any of the claims 1 to 10~~, wherein said stabilizer comprises a substance selected from the group consisting of polysorbate 85, dextran 12.000, carboxylic acid esters of multifunctional alcohols, polysorbates, polyoxameres, polyoxamines, alkoxylated ethers, alkoxylated esters, alkoxylated mono-, di and triglycerides, alkoxylated phenoles and diphenoles, substances of the Genapol^{R} and Bauki^{R} series, metal salts of carboxylic acids, metal salts of alcohol sulfates and metal salts of sulfosuccinates and mixtures of two or more of said substances.

12. The drug targeting system according to claim 11, wherein said stabilizer comprises a substance selected from the group consisting of polysorbate 85, polysorbate 81, dextran 12.000, carboxylic acid esters and preferably fatty acid esters of glycerol and sorbitol, even more preferably glycerol monostearate, sorbitan monostearate and sorbitan monooleate, poloxamer 188 (Pluronic^{R} F68), ethoxylated ethers, ethoxyl-ated esters, ethoxylated triglycerides, ethoxylated phenoles and diphenoles, metal salts of fatty acids and metal salts of fatty alcohol sulfates, preferably sodium salts of fatty acids and of fatty alcohol sulfates,

even more preferably sodium stearate and sodium lauryl sulfate and mixtures of two or more of said substances.

13. The drug targeting system according to claim 12, wherein said stabilizer comprises a substance selected from the group consisting of polysorbate 85 or dextran 12.000 and mixtures thereof and mixtures of said stabilizers with other stabilizers.

14. The drug targeting system according to ~~any of the claims 1 to 13~~ claim 1, wherein said carrier and/or diluent is/are selected from the group consisting of water, physiologically acceptable aqueous solutions containing salts and/or buffers and any other solution acceptable for administration to a mammal.

15. A method for preparing a drug targeting system for administering one or more physiologically effective substance(s) to a mammal, said method comprising the steps of

- preparing nanoparticles made of a polymeric material, said nanoparticles comprising said polymeric material, one or more physiologically effective substance(s) to be delivered to said mammal and one or more stabilizer(s) for said nanoparticles allowing targeting of said physiologically effective substance(s) to a specific site within or on a mammalian body, by polymerizing, in a per se known manner, one or more monomeric and/or oligomeric precursor(s) of said polymeric material in the presence of said physiologically effective substance(s) and in the presence of said stabilizer(s); and optionally
- providing said nanoparticles in a medium allowing the transport of said nanoparticles to a target within or on said mammal after administration.

16. A method for preparing a drug targeting system for administering one or more physiologically effective substance(s) to a mammal, said method comprising the steps of

- preparing nanoparticles made of a polymeric material, said nanoparticles comprising said polymeric material and one or more stabilizer(s) for said nanoparticles, by polymerizing, in a per se known manner, one or more monomeric and/or oligomeric precursor(s) of said polymeric material in the presence of said stabilizer(s);
- loading one or more physiologically effective substance(s) to be delivered to said mammal into and/or onto said nanoparticles; and optionally
- providing said loaded nanoparticles in a medium allowing the transport of said nanoparticles to the target within or on said mammal after administration.

17. The method according to ~~claims 15 or 16,~~ Claim 15 wherein said polymerization step is selected from the group consisting of emulsion polymerization, interfacial polymerization, solvent deposition, solvent evaporation and crosslinking oligomers and/or polymers in solution.

18. The method according to ~~any of the claims 15 to 17,~~ Claim 15 wherein, in the polymerization step, a polymeric material is formed which is selected from the group consisting of polyacrylates, polymethacrylates, polycyanoacrylates, polyarylamides, polylactates, polyglycolates, polyanhydrates, polyorthoesters, gelatin, polysaccharides, albumin, polystyrenes, polyvinyls, polyacrolein, polyglutaraldehydes and derivatives, copolymers and mixtures thereof.

19. The method according to ~~any of the claims 15 to 18,~~ Claim 15 wherein said loading step comprises mixing said nanoparticles with a solution of said physiologically effective substance(s) and allowing a sufficient time for an effective amount of said physiologically effective substance(s) to be adsorbed onto and/or absorbed by said nanoparticles.

20. The method according to ~~any of the claims 15 to 19,~~ Claim 15 wherein as said stabilizer(s) for said nanoparticles, there is/are used one or more substances selected from the group consisting of stabilizers which allow a passage of said nanoparticles including said physiologically effective substance(s) through the blood brain barrier in said mammal and stabilizers which allow a release of said physiologically effective substance(s) from said

nanoparticles and a passage of said physiologically effective substance(s) through the blood brain barrier separate from said nanoparticles.

21. The method according to claim 20, wherein as said stabilizer(s), there is/are used one or more substances allowing a passage of said physiologically effective substance(s) through the blood brain barrier without chemical modification of said physiologically effective substance(s).

22. The method according to ~~any of the claims 15 to 21~~ Claim 15, wherein as said stabilizer(s), there is/are used one or more substance(s) selected from the group consisting of polysorbate 85, dextran 12.000, carboxylic acid esters of multifunctional alcohols, polysorbates, polyoxameres, polyoxamines, alkoxylated ethers, alkoxylated esters, alkoxylated mono-, di and triglycerides, alkoxylated phenoles and diphenoles, substances of the Genapol^{R} and Bauki^{R} series, metal salts of carboxylic acids, metal salts of alcohol sulfates and metal salts of sulfosuccinates and mixtures of two or more of said substances.

23. The method according to claim 22, wherein as said stabilizer(s), there is/are used one or more substance(s) selected from the group consisting of polysorbate 85, polysorbate 81, dextran 12.000, carboxylic acid esters and preferably fatty acid esters of glycerol and sorbitol, even more preferably glycerol monostearate, sorbitan monostearate and sorbitan monooleate, poloxamer 188 (Pluronic^{R} F68), ethoxylated ethers, ethoxylated esters, ethoxylated triglycerides, ethoxylated phenoles and diphenoles, metal salts of fatty acids and metal salts of fatty alcohol sulfates, preferably sodium salts of fatty acids and of fatty alcohol sulfates, even more preferably sodium stearate and sodium lauryl sulfate and mixtures of two or more of said substances.

24. The method according to ~~claims 22 and 23,~~ Claim 22 wherein as said stabilizer(s), there is/are used one or more substance(s) selected from the group consisting of polysorbate 85 and dextran 12.000 and mixtures thereof and mixtures of said stabilizers with other stabilizers.

25. The method according to ~~any of the claims 15 to 24,~~ Claim 15 wherein as said physiologically effective substance(s), there is/are used one or more substance(s) selected from the group consisting of a therapeutic agent and a diagnostic agent.

Claim 15

26. The method according to ~~any of the claims 15 to 25,~~ wherein as said physiologically effective substance(s) there is/are used a substance/substances which has/have central nervous system activity but cannot cross the blood brain barrier without modification or without a carrier.

Claim 15

27. The method according to ~~any of the claims 15 to 26~~, wherein as said drug, there is/are used a substance/substances selected from the group consisting of drugs acting at synaptic sites and neuroeffector junctional sites; general and local analgetics; hypnotics and sedatives; drugs for the treatment of psychiatric disorders such as depression and schizophrenia; anti-epileptics and anticonvulsants; drugs for the treatment of Parkinson's and Huntington's disease, aging and Alzheimer's disease; excitatory amino acid antagonists, neurotrophic factors and neuroregenerative agents; trophic factors; drugs aimed at the treatment of CNS trauma or stroke; drugs for the treatment of addiction and drug abuse; antacoids and anti-inflammatory drugs; chemotherapeutic agents for parasitic infections and diseases caused by microbes; immunosuppressive agents and anti-cancer drugs; hormones and hormone antagonists; heavy metals and heavy metal antagonists; antagonists for non-metallic toxic agents; cytostatic agents for the treatment of cancer; diagnostic substances for use in nuclear medicine; immunoactive and immunoreactive agents; transmitters and their respective receptor agonists and receptor antagonists, their respective precursors and metabolites; transporter-inhibitors; antibiotics; antispasmodics; antihistamines; antinauseants; relaxants; stimulants; sense and antisense oligonucleotides; cerebral dilators; psychotropics; antimanics; vascular dilators and constrictors; anti-hypertensives; drugs for migraine treatment; hypnotics, hyperglycemic and hypoglycemic agents; minerals and nutritional agents; anti-obesity drugs; anti-asthmatics; and mixtures thereof.

Claim 15

28. The method according to ~~any of the claims 15 to 26~~, wherein as said diagnostic agent, there is/are used a substance/substances selected from the group consisting of diagnostics useful in the diagnosis in nuclear medicine and in radiation therapy.

Claim 15

29. The method according to ~~any of the claims 15 to 28,~~ wherein said medium allowing the transport of said nanoparticles to the target within said mammal after administration is selected from the group consisting of water, physiologically acceptable aqueous solutions

containing salts and/or buffers and any other solution acceptable for administration to a mammal.

30. The drug targeting system according to ~~any of the claims 1 to 14~~ Claim 1 for medical use.

31. Use of the drug targeting system according to any of the claims 1 to 14 in the preparation of a medicament allowing one or more physiologically effective substance(s) to be targeted to a specific site within or on a mammalian body.

32. Use of the drug targeting system according to ~~any of the claims 1 to 14~~ Claim 1 in the preparation of a medicament allowing one or more physiologically effective substance(s) to be delivered across the blood brain barrier of a mammal.

33. Use of the drug targeting system according to ~~any of the claims 1 to~~ Claim 1 14 in the preparation of a medicament achieving a pharmacological effect in the central nervous system of a mammal.

34. Use of the drug targeting system according to ~~any of the claims 1 to 14~~ Claim 1 in the preparation of a medicament achieving a pharmacological effect in the central nervous system of a mammal by the action of one or more physiologically effective substance(s) otherwise not passing the blood brain barrier.

35. Use of the drug targeting system according to ~~any of the claims 1 to 14~~ Claim 1 in the preparation of a medicament achieving a pharmacological effect in the central nervous system of a mammal by the action of one or more physiologically effective substance(s) otherwise passing the blood brain barrier in an amount being not or not sufficiently pharmacologically effective.

36. Use according to ~~any of the claims 30 to 35~~ Claim 30 in the preparation of a medicament being adapted for an oral, intravenous, subcutaneous, intramuscular, intranasal, pulmonal or rectal administration, preferably for the oral or intravenous administration.

Claim 30

37. Use according to ~~any of the claims~~ 30 ~~to 36~~ in the preparation of a medicament for administration to a human.

38. A method of targeting one or more physiologically effective substance(s) to a specific target within or on a mammalian body, wherein a drug targeting system according to ~~any of the claims 1 to 14~~ is administered to a mammal.

Claim 1

39. The method according to claim 38, wherein a passage of one or more physiologically effective substance(s) through the blood brain barrier is effected by administering said drug targeting system to said mammal, preferably to a human, and allowing a sufficient time to pass until a pharmacologically effective amount of said physiologically effective substance(s) has passed the blood brain barrier.

Claim 38

40. The method according to ~~claims 38 and 39,~~ wherein said administration is effected on an oral, intravenous, subcutaneous, intramuscular, intranasal, pulmonal or rectal route, preferably on the oral or intravenous route.

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